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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/714,692	11/16/00	LEE K	D6233CIP

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EXAMINER	
BUNNER, B	
ART UNIT	PAPER NUMBER
1647	5

DATE MAILED: 08/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Offic Action Summary	Application No. 09/714,692	Applicant(s) LEE ET AL.	
	Examiner Bridget E. Bunner	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *1-19 and 24-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-27* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Substitute PTO-948* .

DETAILED ACTION

The Art Unit location and the examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1647, Examiner Bridget E. Bunner.

Election/Restrictions

Applicant's election without traverse of Group VIII, claims 20-23, drawn to protein therapy to inhibit angiogenesis in Paper No. 4 (28 June 2001) is acknowledged.

Claims 1-19 and 24-27 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 4 (28 June 2001).

Drawings

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Specification

1. The disclosure is objected to because of the following informalities:

1a. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "METHOD OF INHIBITING ANGIOGENESIS BY ADMINISTRATION OF A CRFR2 AGONIST".

1b. The Brief Description of the Drawings for Figure 1D refers to staining in the cortex, symbolized as (C) on the Figure. However, the letter (C) is not visible on Figure 1D.

1c. The Brief Description of the Drawings only refers to Figures 4A-4D. However, there are Figures 4A-4H in the application. Also, the individual descriptions for Figures 4A-4D do not appear to match the graphs represented in Figures 4A-4D.

1d. The Brief Description of the Drawings for Figure 6 only describes two of the bars on the graph. It cannot be determined what the third bar represents.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 20-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 20-23 are directed to a method of inhibiting angiogenesis in a target tissue comprising administering a CRFR2 agonist to an individual having a pathophysiological condition selected from the group consisting of cancer and diabetic retinopathy. The claims also recite that the CRFR2 agonist is selected from the group consisting of urocortin and CRF and the target tissue is selected from the group consisting of heart, brain, pituitary, gonad, kidney, adipose, and gastrointestinal tract tissues.

The specification teaches that "CRFR2 null mutant mice appeared to exhibit an increase in the size and number of blood vessels in various tissues. Since the CRFR2 receptor and its

activity have been localized within the endothelial cell layer of blood vessels, it was hypothesized that CRFR2 may play a role in regulating angiogenesis" (pg 48, lines 20-21; pg 49, lines 4). The specification also discloses that immunostaining is performed to confirm that CRFR2 null mutant mice had an increased number of blood vessels of larger size. Further, the specification teaches that "one of the roles of the CRFR2 receptor in normal mice is to mediate a CRF-induced inhibition of angiogenesis" (pg 50, lines 16-18). Additionally, the specification discloses that CRFR2 appears to be involved in angiogenesis in fully developed mice rather than embryonic mice (pg 51). However, the specification does not disclose any methods or working examples to demonstrate that CRFR2 agonists, particularly urocortin and CRF, are able to inhibit angiogenesis in any target tissue or in any individual with any pathophysiological condition. Undue experimentation would be required of one skilled in the art to determine the route of administration of the agonist, as well as quantity and duration of treatment and any possible side-effects experienced by the individuals in the study. Relevant literature reports that many anti-angiogenic therapies, particularly for treating cancer, were highly active in animal models, but clinical results so far have been disappointing (Griffioen et al., Pharmacological Reviews 52(2): 237-268, 2000; pg 261, col.1, lines 1-2). Furthermore, in pathophysiological conditions, such as tumors, the percentage of proangiogenic vessels is variable, often quite low, and hence anti-angiogenic therapy may only affect a minority of vessels (Griffioen et al., pg 262, pp 1). Additionally, strategies to target specific stages of disease progression require "an enormous preclinical research effort on the most potent formulations, dosing regimens, and so on" (pg 262, pp 1).

Due to the large quantity of experimentation necessary to inhibit by administration of a CRFR2 agonist and to determine the route, quantity, and duration of administration of the agonist, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, the contradictory state of the prior art (see Griffioen et al.), and the unpredictability of the effects of a CRFR2 agonist on angiogenesis inhibition, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 USC § 112, second paragraph

3. Claims 20-23 are indefinite because the claims do not have a step that clearly relates back to the preamble. For example, there is no step indicating that the CRFR2 agonist inhibits angiogenesis.

4. Regarding claims 20-23, the acronyms "CRFR2" and "CRF" render the claims vague and indefinite. Abbreviations should be spelled out in all independent claims for clarity.

Conclusion

No claims are allowable.

The art made of record and not relied upon is considered pertinent to applicant's disclosure:

Perrin et al. J. Pharmacol. Exp. Therapeutics 288: 729-734, 1999.

Arbiser et al. J. Investigative Dermatology 113(5): 838-842, 1999.

Schilling et al. Brit. J. Pharmacol. 125: 1164-1171, 1998.

Schoeffter et al. Fundam. Clin. Pharmacol. 13: 484-489, 1999.

Villalona-Calero et al. Annals of Oncology 9:71-77, 1998.

Britton et al. Brain Res. 369: 303-306, 1986.

Menzaghi et al. J. Pharmacol. Exp. Therapeutics 269: 564-572, 1994.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

BEB
Art Unit 1647
August 7, 2001

ELIZABETH KEMMERER
PRIMARY EXAMINER